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THE Southern Practitioner

AN INDEPENDENT MONTHLY JOURNAL

DEVOTED TO MEDICINE AND SURGERY.

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DEERING J. ROBERTS, M.D.,

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Original Communications.

CHARGE TO THE GRADUATING CLASS, UNIVERSITY OF TENNESSEE MEDICAL DEPARTMENT.

BY HILLIARD WOOD, M. D., OF NASHVILLE, TENN.

Gentlemen of the Graduating Class—

The time has come when those of you who have completed the curriculum and successfully passed your final examinations shall receive your diplomas, which shall be to the public the evidence of your proficiency. I congratulate you, gentlemen of the graduating class, upon this happy conclusion of your college course, and upon having won, by a rigorous examination, this degree which shall admit you to broader fields of study and of usefulness. For four long years your devotion to every detail

of your college work, and the enthusiasm which has marked your pursuit of medical knowledge constitute a favorable augury and happy omen of that successful career which, I trust, in the not distant future awaits each one of you.

From the day of your matriculation to this happy hour your thoughts have been fixed upon these certificates of your worth which you now have fairly won, and which it is the pleasure of your faculty you shall receive. Your college course has been both long and arduous; to it you have devoted laborious days and sleepless nights; your studies have been difficult and often technical, but the trials through which you are now happily passed have only exercised your devotion and demonstrated your zeal. Your faculty have closely watched, with feelings of mingled solicitude and admiration, the spirit in which you have discharged every duty, have mastered every subject, and have met every obligation placed upon you. Such moral worth and mental ability give birth to hopes of greater achievements still. It is, therefore, not grudgingly, or with reluctance, that we give you these diplomas, but with joy, believing that what you have by merit won, you will, by virtue, honor.

Although tonight you complete your college course, your education as members of a learned profession is far from complete. This you will notice as soon as you have entered the field of practice; for here you will meet with diseases that puzzle you, and complications which baffle your best endeavors. Thus, humbled by defeat and saddened by disappointment, your only safeguard and remedy will be found in earnest, patient, unremitting labor and study. These are the agencies which have helped others before you to higher planes of glory and broader fields of usefulness, and constitute the only "*sesame*" which can unlock to you the treasure-house where fame and knowledge dwell. No matter how high a record you may have made in your classes, how enviable a reputation you may have maintained with your faculty, or how auspicious may be your entrance upon a professional career, unremitting study and perseverance are essential, if you would keep abreast of the progressive and exacting science of medicine. The man who does less can not

reasonably hope, and does not deserve, to retain the confidence and patronage of the public, or the esteem of his fellow physicians.

In the pursuit of medical knowledge you have, so far, drawn only from two sources, from your teachers and from your text-books. To these is now to be added a third and a larger supply —that is from the observation of nature, or from practice. This is the spring and fountainhead of all medical knowledge. So far you have been fed, as it were, with pre-digested food, but now you are to be fed with meat of the profession that you may grow strong. This meat is the observation of the patient in the sick room. Here you will learn your most valuable lessons, and here you will be subjected to the final test by which you must either stand or fall as a physician. Your study of your patient and his disease and the proper interpretation of the signs and symptoms will determine your success in practice. I do not mean to underrate the writings of the great men in our profession; these writings should be the subject of your daily and careful study. They have their value, but their value has its limit. You should believe and follow them in so far as they accord with nature, but no farther. Strictly speaking no man is an authority in medicine, although some are so styled, and vanity has induced some to so style themselves; but there is one, and only one authority in medicine, and that is the authority of nature. The more carefully you study that, the closer you keep to that, the better able you are to interpret that, the more successful you will be as physicians. No stream rises above its source, and no one learns more by reading a book than the writer knew. If, therefore, you would surpass in medical knowledge you must not only know the literature, but you must know nature, and from that pure and inexhaustible source draw fresh supplies.

Medical literature is not an end, but a means, a light to guide you in your search for truth. With the best literature, therefore, you should be always familiar. But you should use it as a crutch to help your understanding, not as a shackle to bind your mind, or to prevent independent thought. Medical progress through the ages has been marked by great discoveries. If we

study any one of these we find a man close to the heart of nature who, discarding dogma, has interpreted nature, and has interpreted it wisely. With what admiration and despair do we look upon these men; and yet any one of us, did we but use the same means might attain the same end. But originality is a virtue of the few, imitation a characteristic of the many. Gentlemen, I would have you study nature, I would have you study disease as it is found in your patient, not simply read it as it is written in your books. Nature is the great text-book, nature alone is infallible. To study it, to commune with it, to know it, should be your constant aim and effort. This alone can raise you above the dull monotony of routine to sublimer heights and grander views.

You should be not only ambitious to acquire, but also glad to communicate medical knowledge. You should be like a pump which not only receives, but also gives out. Medical knowledge has made its slow, and often intermittent progress through the ages. The present sum of this knowledge represents the observation, experience and wisdom of the centuries that are past. This is a precious heritage, and is offered to us practically without money and without price. The great men who have gone before have, by superior wisdom, projected themselves into the generations which followed them, and have made our present achievements possible. We are the heirs of all the past, and should show our appreciation of this priceless inheritance by gratitude to those who have gone before, and by our constant effort to add to the sum of medical knowledge that we, like them, may project ourselves into the generations which are to come.

Medicine is not a fixed, but a progressive science; and our knowledge of it, so long as we remain in the practice, should likewise progress. The constant acquisition of knowledge is one of the most pleasant experiences in the practice of medicine. It is food to the mind, it nourishes and makes strong; it is like refreshing showers upon parched ground, it gives new energy, and life, and hope. The mind may be compared to a sieve, into which information is poured, but through which, by defective memory, it leaks; so that if we would keep it filled we must

constantly add more. It is but due to your patient and to yourself that you should be the best doctor of which you are capable.

Pleasure in any avocation of life is in proportion to the excellence we attain in it. Merit breeds success, and success, happiness. Happiness is, therefore, based upon our merit, and this is wise. If we would have happiness, therefore, we must deserve it; and we can not deserve it without the approval of our conscience, that censor from which no secrets are hid.

Zeal and faith are as essential to the practice of medicine as fuel and steam are to the operation of a locomotive. If I had a mental thermometer, by which I could tonight test your zeal for medicine, I would know your medical future, as to who will fail and who will succeed. Zeal for a cause and faith in it, a willingness to toil for it, and if need be, to suffer for it, are the conditions of success. It has been said that no great movement ever succeeds unless some one is willing to suffer for it. We know that all great reformations have demanded toil and usually blood. Sacrifice and self-denial have ever been the price of achievement. If you would succeed in medicine you must be willing to spend and to be spent for it; you must be willing to toil, and, if need be, to suffer for it. I do not know any medical man of prominence who is not in a very material sense a slave to his profession. It is the price of his success.

Medicine will need and demand your full time; you can not successfully divide your attention between it and other pursuits; you can not at the same time be a good doctor and a good farmer or a good merchant. You will fail in one or the other, or more likely in all. Neither can the practice of medicine be laid down for a term of years and afterward successfully resumed. When once deserted it seldom, or never, returns. Medicine is exacting, demanding your whole time and thought, leaving you little opportunity to mingle in social or business life. Doctors are, therefore, known as poor business men, and are regarded as easy marks by the shrewd and, apparently, innumerable promoters of wild-cat schemes and mining companies. So poorly remunerative is medicine and so long and difficult is the

acquirement of a competency by practice that when a physician has saved up a few dollars it would seem he might be permitted to enjoy it at pleasure; but no sooner is a doctor suspected of having a dollar than his desk is flooded with the alluring literature of get-rich-quick concerns, and he is invited and actually expected to pour into this yawning chasm that which, he had hoped, would protect his age from poverty and want. And the sad thing about it is, that the doctor actually does it, and is then surprised when he discovers he has purchased a brick of a golden hue. We doctors inveigh against quack nostrums and patent medicines, and yet do we not fall victims to all the forms of financial quackery that are presented for the delectation of the credulous public? We are amused at patients who invest their money in patent medicines, and then are, ourselves, taken in by the first financial charlatan who comes along, and invest our money in visionary schemes that exist only, if they exist at all, in the fertile imagination of the promoter.

In delivering to you, gentlemen, this last charge of your faculty, I am filled with emotions of mingled hope and fear—of hope for your enduring success, and of fear lest the innumerable sources of error and defeat, often half hidden and concealed, may "Turn your day of youth to sullied night." As a mariner, traversing the wide waste of ocean, trusts not his feelings, but fixes his eyes upon his compass and upon the fixed stars and heavenly bodies and by their aid reaches in safety the haven of his desire, so you, traversing the tempestuous sea of life, with its ever shifting scenes, will do well to lay aside your prejudices and passions, and be guided only by those wise precepts and sage maxims which have been handed down to us by history. Churches have creeds, political parties platforms, and medicine has its code of ethics. I commend to your careful study and constant practice "The Code of Ethics of the American Medical Association." This code is based upon the Golden Rule, and in it is epitomized your various duties and obligations to your patient, your brother physician and yourself. By closely following its provisions you will exercise those virtues which, not only promote happiness, but which develop in you those

qualities of mind and heart that contribute most to your usefulness and success. It breathes the spirit of brotherly love and charity. It teaches you that your brother physician has the right to expect as much of you as you do of him. How essential to the greatest good of any organization or profession is the mutual confidence and cohesion of its members! How essential it is to the greatest good of medicine! I do not know of anything that so softens the asperity of our criticisms of the faults of others as silent reflection upon our own.

"When to the sessions of sweet silent thought
I summon up remembrance of things past,
I sigh the lack of many a thing I sought."

Solitude and introspection teach us that we have need of that charity which we are often so slow to extend to our brother. The words of criticism which we utter against another are more often an index to our character than a measure of his faults. How slow are we to recognize that the mind begets thought, thought begets action, action begets habit, habit begets character, and character is what we are! Show me a man's thoughts and I know what he is. As we think so we are. When we speak evil of our brother physician how blind we are to the fact that we only advertise the evil that is within us. I charge you, therefore, gentlemen, that you speak no evil one of another, but that at all times and in all places you defend the high character of your profession and of its members, knowing full well that by so doing you will receive that reward which your merit deserves.

Young gentlemen, there are within you faculties which, with proper evolution, shall develop into mighty forces for good. See that these God-given properties of mind and soul do not lie dormant and decay for want of use, but that they are developed by judicious exercise into a manly, Christian character. Your life will be spent with the sick, the suffering and, at times, the dying. Do all in your power to develop the qualities of gentleness, sobriety, and strict moral integrity, that you may win, deserve

and retain the respect and confidence of those whose lives shall be entrusted to your care.

You will soon depart for the society of your loved ones and the scenes of your future labors. As you go, remember you leave behind you in Nashville twelve men who feel as fathers feel, and who shall share alike your joy and grief. No more we meet in hospital clinics or college halls. We who lately met as professor and pupil now part as brothers.

Gentlemen—

"I charge you fling away ambition;
By that sin fell the angels, how can man then,
The image of his Maker, hope to win by't?
Love thyself last: cherish those hearts that hate thee;
Corruption wins not more than honesty.
Still in thy right hand carry gentle peace,
To silence envious tongues. Be just, and fear not:
Let all the ends, thou aim'st at, be thy country's,
Thy God's, and truth's; then if thou fall'st,
Thou fall'st a blessed martyr."

Selected Articles.

THE AUTO-PROTECTIVE RESOURCES OF THE BODY —A NEW FOUNDATION FOR SCIENTIFIC THERAPEUTICS.*

BY CHARLES E. DE M. SAJOUS, M.D., PHILADELPHIA.

In acknowledging the honor your Executive Committee has conferred upon me by inviting me to address you this evening, Mr. President and Gentlemen, I must apologize for the many allusions

*Read by invitation before the American Therapeutic Society, and the Philadelphia Branch of the American Pharmaceutical Association, May 7, 1908, and reprinted from advance sheets of *The Monthly Cyclopedia of Practical Medicine.*

to personal investigations that my remarks will contain. The reason for this seeming selfishness is readily accounted for: your committee believed that the newer conception of pharmacodynamics I have to offer, might prove of some interest not only to the members of the Therapeutic Society, but also to those of the pharmaceutical profession, whom it gives us pleasure to welcome this evening.

Prof. John H. Musser, in a paper published three years ago in the *American Journal of Pharmacy*, stated that "just as the present compares with twenty years ago, one can see less and less of the use of drugs." While predicating from this deduction that twenty years hence "a minimum of drugs" would be used, he cited broncho-pneumonia and tuberculosis as examples of the value of rest, fresh air, and proper food. Sir Frederick Treves more recently gave vent to similar views; while recognizing that "the habit of taking medicines lies deep down in the hearts of the people," he, too, thought that the use of drugs would "be replaced by simple living, suitable diet, plenty of sun, and plenty of fresh air." Similar conclusions are often published by men of high standing. And yet can they, in truth, dispense with drugs? No experienced practitioner will deny that nine-tenths of our professional usefulness is based on pharmaceutical remedies. Not only do our patients crave active, militant protection and relief in the hour of suffering, but the physician knows through the teachings of practical experience that drugs are his legitimate and often trustworthy weapons of warfare, the strongest shield he has to interpose between his patients and the fell destroyer.

Closely allied to the air, food, and water apostles are the therapeutic nihilists who, like Professor Osler, believe in the doctrine of self-limited diseases and look on while Nature and the disease have it out. Dr. Abraham Jacobi who, in accord with the great bulk of the profession, considers expectancy as a synonym for loss of time and opportunity, characterizes this nihilistic attitude as a compound of ignorance and indolence, and as "a sin of omission which frequently arises to the dignity of a crime." Emphasizing, moreover, the truth of Dixon's doctrine that the tendency of all diseases is toward death, he urges—and sustains

by illustrative cases—that lack of timely treatment is accountable for much loss of life. Indeed, we blame, and our courts sometimes punish mystic therapeutists, Christian scientists, etc., for similar reasons, and it becomes a question whether their attempt to afford some help does not exonerate them in the presence of our own therapeutic pessimists who supply nothing—except, perhaps, a correct death certificate if the patient happens to die.

Another most regrettable feature of present-day medicine is that public confidence in our professional efficiency is on the wane, as the frequent attacks in the lay press well attest. Disregarding totally the many sides of our professional work which should command appreciation, the incalculable benefits that thousands of noble and self-sacrificing men have bestowed upon humanity, many who, in the moment of danger, at once seek our aid are not loathe to lapidate us when the occasion offers. Other countries, even the great European centers of learning, are equally militant. Thus, Professor Dieulafoy, of Paris, declared only a few months ago, that medical men are criticised on all sides: in public, in the drawing-room, at dinner parties, on the stage, in the newspapers, etc., and that books, even, are written expressly to condemn the medical profession! The normal results of this campaign are that a multitude of innocent people are increasingly driven into the hands of quacks; that systems of practice based on mysticism and misrepresentation are steadily gaining ground, and that patent medicine vendors are accumulating untold wealth at the expense of the unwary.

What is the underlying cause of all this? An analysis of the causes of defection in our own ranks is, I believe, first in order. Indeed, as stated by Llewellys F. Barker in 1900, at the close of a century during which all sciences other than medicine had advanced at an amazing pace: "With many, pharmacotherapy, as a whole, is almost moribund."

Shall, we, however, with Dr. Jacobi and other distinguished men of our profession, ascribe to ignorance the loss of confidence in remedies that some of its members betray? What physician would presume to assert that mercury in syphilis, quinine in malaria, iron in simple anæmia, arsenic in pernicious anæmia, thyroid

extract in cretinism and myxœdema, antitoxin in diphtheria, digitalis in certain cardiac disorders, sodium salicylate in muscular rheumatism, strychnine in adynamia, and many other remedies I could cite, are useless? And yet, Dr. Frank Billings wrote, in 1903, that "drugs, with the exception of quinine in malaria, and mercury in syphilis, are valueless as cures;" in 1907 these last vestiges of our glory must have vanished, for the president of a prominent British society, Dr. A. H. Brampton, took occasion to say, as a prelude to a personal expression of dissent: "Skepticism is in the air. Even in this society, if any daring member has introduced a subject bearing on medical treatment, it has been with an apologetic air and humble mien, well knowing that if his remarks had any reference to the utility of drugs in the treatment of disease, they would be subject to good-humored banter, and received by those sitting in the seat of the scornful with amused incredulity." May we not be dealing with an unwarranted prejudice against drugs rather than with ignorance? Again is it not among the best informed men of our profession that drug-nihilism prevails pre-eminently?

It should be attributed, it seems to me, to an entirely different cause—one, indeed, which is increasingly making itself felt from day to day. Bichat said over a century ago, "pharmacology, in its present state, is not a science fit for a methodic mind." Notwithstanding the enormous painstaking labor that has been devoted to the multitude of problems it offers, Bichat's estimate is still applicable—a fact emphasized by the oft repeated admission that therapeutics has not raised itself above the level of empiricism.

We all know, for example, that mercury is curative in syphilis; but how is this accomplished? This, as Manquat asserts in the last edition of his *Therapeutics,* "is impossible to say." Another mainstay in many diseases is iodine, not only the haloid proper, but its salts. Hare writes: "The physiological action of iodine, so far as its alterative powers are concerned, is absolutely unknown." The brightest star of late-date therapeutics, antitoxin, stands not a whit higher. H. C. Wood, after reviewing the more familiar theories of its action, including Ehrlich's theory, says: "It must be confessed that we have no positive knowledge

of the manner in which this substance acts in infectious diseases." Another truly wonderful agent—particularly in myxœdema and cretinism—is thyroid extract, but, as to its mode of action, Laulanie tells us that "for the time being there is not even a clue to the solution of this problem." As to digitalis, H. C. Wood, Sr. and Jr., write: "In our experiments upon the exposed mammalian heart, we have seen in the final acts of the digitalis drama happenings so curious that at present no proposed theory as to the action of the drug is sufficient." This obscurity applies more or less to all drugs administered internally.

On the whole pharmacology, which, as shown by Bichat's contemptuous remark, was in a deplorable condition early last century, was still, at its close, notwithstanding an enormous aggregate of sound scientific facts contributed by a host of brilliant scientists, "in a backward and unsatisfactory condition," as a great clinician, Sir Andrew Clark, once expressed it. Indeed, no one can deny that it has failed to keep pace with the other branches of medicine: diagnosis, physiological chemistry, histology, etc., which have steadily gained for themselves a place among the medical sciences. Although the most important of all, and the one branch through which the public, the whole world, in fact, gauges our actual professional efficiency, therapeutics has ever remained a mere art. A remedy is still given because it has been found more or less efficacious in this or that condition by others, and the subdivisions headed "treatment" or "therapeutics" in our text-books are mere catalogues of drugs which are stated to be "particularly useful," "most efficient," "very valuable," "commonly employed," "of great value," etc., in this or that disease, and in which not an inkling is afforded as to *how* the remedy antagonizes the morbid process. Not only does this entail a source of error at every step, since it often happens that a drug indicated in one stage of the disease may be contra-indicated in another, but it leaves the conscientious physician in constant anxiety lest the agent prescribed empirically prove more harmful than beneficial. Hence the frequent, sometimes daily, change of remedies—to which shelves covered with pill boxes and small bottles attest—and, I may add, the ill repute into which therapeutics has fallen.

Need we wonder that highly trained men, who have developed great keenness as diagnosticians and the highest attainable proficiency in pathological histology and chemistry, have lost faith in pharmacotherapy? Are we justified in attributing to ignorance their loss of faith in a system of administering remedies which is as irrational and archaic as the other departments of medicine are precise and modern? Indeed, it is merely *because pharmacotherapy has not kept pace with the immense strides of all other branches that it is, with many physicians,* as stated by Prof. Llewellys F. Barker, *"almost moribund."*

Next in order is the cause of this deplorable condition of therapeutics. Must we attribute it to the host of investigators in pharmacodynamics to whom I have referred? Even though experimental errors to which I will allude presently, might have delayed progress, I firmly believe that if there had not been insuperable obstacles in another direction, therapeutics would stand today among the most advanced medical sciences as a result of their labors. One of their number, the foremost sponsor of experimental therapeutics of our day, Horatio C. Wood, Sr., of our own city, and several equally eminent foreign colleagues, would long ago have given us a sound foundation for the intelligent use of drugs had their deductive reasoning not been handicapped at every step, by a feature of the question to which I called attention last year: *the shortcomings of physiology.*

To interpret intelligently the physiological action of alteratives and tonics, which are in daily use by physicians, for example, an accurate knowledge of general metabolism, the foundation of nutrition, is necessary. What is known on this subject, according to the late Sir Michael Foster, "consists mostly of guesses and gaps." The action of cardiac stimulants includes as a main phenomenon slowing of the heart through the mechanism of inhibition. Physiologists, according to Langley, "are still far from any real knowledge of the processes involved in inhibition." Diaphoretics and sialagogues activate the sweat and salivary glands by causing vaso-dilation in these organs. As Chapman says: "Though numerous explanations have been offered of the manner in which the vaso-dilator nerves act, it must be admitted

that none of them are satisfactory." The study of hypnotics and anæsthetics presupposes a knowledge of the process through which sleep is produced. According to Bradbury "the phenomenon is still enveloped in mystery." Analgesics and nerve sedatives and stimulants owe their action to modifications in the character of the impulses awakened in the nerves; but as Stewart says, "what the nerve-impulse actually consists in we do not know." This factor is intimately linked, in the action of antispasmodics and convulsivants, with muscular oxidation, but Laulanie writes "we are absolutely ignorant of the mechanism of organic oxidation." Purgatives, whether their effects be due to an increase of secretory or peristaltic activity evoke them through secretory or motor nerve-paths; but, as Langley states, the relation of the enteric nervous system to the cranial nerves "is at present a matter of guesswork." Emetics suggest the need of adequate knowledge of the process of vomiting, but, according to Foster, "the nervous mechanism of vomiting is complicated and in many respects obscure." To explain the action of diuretics the mechanism through which the secretion of urine is governed should be known; "as yet," writes Landois, "only the influence of the vasomotor nerves upon the filtration of the urine from the renal vessels is known"—which means that that of the secretory nerves is not.

In brief, every important subdivision of therapeutics thus finds itself deprived of the essential physiological knowledge upon which a rational explanation of its physiological action could be poised. And this does not apply to therapeutics only; pathology is suffering, and has suffered, all along from the same cause, since, after all, the morbid effects of bacterial toxins or endotoxins, poisons, toxic wastes, etc., act in the body as would poisonous doses of drugs persistently administered.

Is there any indication that physiologists will furnish the data we need to place pharmacology on the sound basis we so earnestly crave? I must frankly express the belief that, judging from present indications, the prospects are very discouraging. In the first place, a cursory glance through physiological literature shows that they devote very little work to the study of the physiological

problems I have enumerated. In the second place they overlook the one source of information through which their own labors could be made promptly to bear fruit: that covered by the assertions of a great Russian physiologist, Professor Pawlow, that in many instances "the physician gives a more correct verdict concerning physiological processes than the physiologist himself," and that "clinical observation will consequently always remain a rich mine of physiological facts." In the third place I greatly regret to say that they are steadily deserting us. A physiologist, Dr. Meltzer, wrote, a few years ago: "Physiology is of medical parentage, was reared by medical men, and is still housed and fed by medical faculties. Still it is medicine against which its frequent declaration of independence is directed. Medicine is a practical science, and is too inexact, and physiology wishes to be a pure, exact science. It, therefore, tries to keep aloof from medicine, and manifests a longing for association with, or, better still, for a reduction to physics and chemistry." Time has only served to sustain this statement and to emphasize my own conviction that medicine, and particularly pharmacology, will not be redeemed from its present deplorable position as long as it will depend entirely upon physiologists for the elucidation of function.

This is not intended to mean that pharmacologists are not also open to criticism. But their shortcomings cannot be ascribed to a lack of effort on their part to elucidate the multitude of problems they are expected to solve; they are due, in my opinion, to errors of procedure and of interpretation in the course of their experimental work.

First among these is the belief that drugs given by the mouth, injected hypodermically or rectally, travel to the tissues and act upon them. Text-books tell us, for instance, that digitalis excites directly the muscular fibers of the heart, and that the rise of blood-pressure and increase of pulse-volume are mainly due to the greater propulsive power with which the drug endows this organ. This is based on experiments in which the heart, partially or entirely detached from the animal, is caused to resume its beats by dropping upon it a solution of digitalin. That this experiment is misleading is suggested by various facts. The weakest solu-

tion that will act directly on the heart thus exposed is 1 part in 50,000. Now, a large therapeutic dose of digitalin by the mouth is 1-4 grain which, dissolved in the blood-mass, would make a solution four times weaker: 1 to 200,000. Hypodermically, 1-16 grain of digitalin produces distinct physiological effects, and yet this is only a solution of 1 to 800,000 in the blood-mass—a solution sixteen times weaker than is absolutely necessary to influence the exposed heart experimentally. The prevailing belief in this connection becomes absurd when to these figures we add the facts that the drug is chemically modified in the blood—when given orally, hypodermically, or rectally—long before it can reach the heart-muscle at all, and that a large proportion of the blood is constantly passing out into the lymph-spaces and vessels, thus necessarily carrying a correspondingly great proportion of the drug with it. Again, why is it, if digitalis acts directly on the heart, that it affects much more actively the right side of this organ than the left? If the blood carried it to the heart-muscle, both sides should be influenced similarly. Another suggestive fact is that division of the spinal cord prevents the effects of digitalis given internally; obviously if the drug acted directly on the heart-muscle, this procedure would not prevent its action. Need we wonder that H. C. Wood, Sr. and Jr., can still say in the last edition of their *Therapeutics* that "at present no proposed theory as to the action of the drug is sufficient"?

There is ample experimental and clinical evidence to show that it is upon the general nerve centers that the vast majority of our drugs act, and that the phenomena witnessed are those awakened by these centers or resulting from diminution or arrest of their functional activity. As stated by Prof. Charles Richet, of Paris, "all toxics (with rare exceptions) are hardly poisonous otherwise than through their action upon the *nerve-cell.* In the organism," adds this distinguished physiologist, "the nerve-cell, to the detriment of other cells: muscular, glandular, epithelial, is the most sensitive to toxic action." Such being the case, the most sensitive nerve-cells, those of nerve centers, are the first to feel the influence of the small doses of toxic that our remedies represent, and it is because of this that such a minute dose of aco-

nitine as 1-400 grain, for example, can depress the whole circulation, and cause muscular torpor and weakness and also, perhaps, tingling in the extremities.

A second experimental error which proves misleading in most instances is the use of anæsthetics in animals in which a remedy is tried. Ergot, for instance, had been regarded as a vaso-constrictor since its action had been at all seriously studied, when certain investigators, basing their assertion on hundreds of experiments, declared that this agent did not cause vascular contraction. But an examination of their work revealed that they used ether as anæsthetic, an agent which, as is well known, is a powerful vaso-constrictor. How could they possibly cause contraction of the vessels with ergot when these blood-channels were already contracted to their utmost limit by the ether?

A third source of error, one which prevents progress in our knowledge of the action of drugs that affect the cardio-vascular system, is the neglect of waste products as factors in the process. Although veratrum viride, for instance, has long been considered a powerful vaso-dilator, capable of causing the blood to accumulate in the deep and large vessels, thus depleting congested organs, recent experiments have suggested that this drug in reality constricts the arteries. But analysis of these experiments shows that the older view is the correct one, and that the vaso-constriction witnessed by the experimenters was not due to the drug. The large dose used had produced so intense a vascular dilation that catabolism of waste-products in the peripheral capillaries had been inhibited; and these wastes being, as is now well known, powerful vaso-constrictors, they overcame the vaso-dilator action of the veratrum viride and produced vaso-constriction.

A fourth and very misleading error is the experimental use of excessive doses in animals to determine the action of a remedy. In a recently reported study of the therapeutic action of potassium iodide, for example, the investigator administered to his animals doses which in man would represent 346 grains! The effects produced by such doses not only fail to exemplify the therapeutic action of the drug, they are those of intoxication. As stated

by Hale White, "when a drug in moderate doses excites a function, in large doses it often paralyzes it." This applies to a large proportion of the experiments on record, and it is to this fact that the present ignorance of their physiological action must, in great part, be ascribed.

A fifth cause of confusion is the belief that because certain drugs, atropine, for example, paralyze nerve endings by acting directly upon them when locally applied, it produces the same effect through a similar process when given hypodermically or orally. If the smallest dose that will evoke a physiological effect when given internally, is used to prepare a solution with the entire blood and lymph (in which the drug also circulates) of a control animal of equal weight, it will be found inert; first, because the solution obtained is entirely too weak, and second, because it is chemically altered by the blood's antitoxic constituents. In the living animal, and particularly in the carnivora, this latter process is far more active than in shed blood, to such a degree in fact that blood drawn from an animal treated to a dose capable of producing marked physiological effects will prove inactive. The physiologists are the principal victims of this class of error—which applies to other alkaloids: pilocarpine, muscarine, nicotine, etc., employed by them, and many conclusions regarded by these scientists as sound are in reality defective and, therefore, misleading.

The sixth and last source of error I will submit is one which doubtless has cost many lives, namely: The assumption that certain phenomena produced by drugs are manifestations of a normal function. Digitalis, for example, is said to slow the heart by stimulating the vagus; that is to say, the mechanism of inhibition —a supposedly physiological function. But there is no ground for this assumption. In the first place, as Porter says, "the nature of the terminal apparatus by which the vagus inhibits the heart is unknown." In the second place, the coronaries and other arteries of the heart, contrary to what physiologists teach, are supplied with vaso-motor nerves, as shown by microphotographs of these nerves in my work on the "Internal Secretions." Now, ample evidence is available to show that all the drugs which slow the heart

do so partly by causing constriction of these cardiac arteries; that is to say, by reducing the volume of blood supplied to the heart wall. We are not witnessing a normal phenomenon, therefore, when under the influence of large doses of various cardiants the heart is slowed, but a morbid effect: weakening of the heart muscle, a factor to which the increased resistance of the general arterial system to the heart's contractions adds a cause of cardiac arrest.

Other examples could be submitted, but these will suffice, with the shortcomings of physiology previously enumerated, to suggest why therapeutics has failed to keep pace with the other branches of medical science; why, in other words, as Professor Sollmann, a medical member of the Council of Pharmacy of the American Medical Association, could write, regretfully doubtless, only last month: "A generation ago therapeutics was an art, promising to develop into a science. At present it cannot be classed as an art, nor as a science; it can only be classed as a confusion."

Need I further urge that new and more fruitful lines of thought are imperatively needed if the true worth of our profession, its humane purpose, and its very existence are to be perpetuated?

I believe that it is fully within our power as pharmacologists to remedy the prevailing state of things and to raise therapeutics to the dignity of a science. At no time in the history of the world has medicine been richer in solidly grounded experimental and clinical facts, precisely those we need to attain this most ambitious of our aims. We hear much of empiricism, the stigma of medicine as an art, but as Huxley once said: "All true science begins with empiricism, though all true science is such exactly in so far as it strives to pass out of the empirical stage." With the means now at our disposal we need only to strive, to eliminate forever from our escutcheon the blemish that "empiricism" implies. Hosts of workers, those to whom Oliver Wendell Holmes referred when he wrote

"Blest is he who knows no meaner strife
Than Art's long struggle with the foes of life,"

have lived a life of devotion to suffering mankind. They may not

have left us as heritage a therapeutic structure, or even the foundation of one, but they have furnished the hewn stones out of which it can be erected. It is for us to build. We may speak of confusion today; but confusion likewise prevails before each pillar, each stone, of any great edifice has found the place assigned to it by the co-ordinating mind of the architect. *Therapeutics needs architects and builders today far more than it does experimenters;* and when that fact will be thoroughly apprehended a new era for medicine as a whole will begin; one that will ultimately lead to the highest of human accomplishments: the mastery of disease in all of its forms.

It is the result of an effort in this direction, begun some twenty years ago, that I am about to outline. Therapeutics may not exist as a science, but a close scrutiny of all the branches of knowledge related to medicine convinced me that with the many sources of error, physiological and pharmacological, I have submitted, once overcome, the aggregate of sound scientific data at our disposal in literature would supply the elements necessary for an accurate knowledge of the action of drugs. Physiology, cytology, embryology, and the more comprehensive branches of which they form part, zoology and botany, physiological chemistry, and other branches, had to be ranascked for what elucidative facts they might contain. I was overwhelmed by the treasures these auxiliary departments of science contained. Clinical medicine especially proved itself, in keeping with the previously-quoted opinion of Professor Pawlow, "a rich mine of physiological facts."

In submitting to you the briefest possible outline of the newer conception of the action of drugs my labors have suggested, I will introduce only what evidence is absolutely necessary to make my meaning clear, referring you for the rest to the two volumes of my work on the "Internal Secretions." During the balance of the hour allotted to this paper, I will lay special stress, however, upon a conclusion which appears of capital importance: that *we should look to the auto-protective resources of the body, and the laws through which drugs influence them, for a scientific therapeutics.* And let me add that I am no longer alone in advocating this principle. In 1903, only a few months after the first volume

of my work had appeared, and before he could have learned its contents, an eminent clinician, Professor Hayem, of Paris, for instance, taught that the tendency of modern practice was to return to the views of Hippocrates, who believed in the *vis medicatrix naturae;* "therapeutic weapons are wanted," declared the French clinician, "which will reinforce the defensive power of the organism." Need I add that the entire trend of medical thought is in this direction; that the study of immunity has captivated the best minds of modern times; Pasteur, Metchnikoff, Pfeiffer, Bordet, Behring, Roux, Ehrlich, and others? I am not departing from the legitimate field of science or of sound judgment, therefore, when I urge that when a disease is due to the presence of pathogenic bacteria, their toxin, toxic wastes, or any other poison, our aim should be to so enhance the defensive properties of the blood with our remedies, that the disease-breeding agents will promptly be destroyed and converted into eliminable end-products.

Granting that the remedies capable of doing this are known, we remain in the realm of empiricism unless we can ascertain how they act; *how,* in other words, the blood is caused by certain drugs to attack and destroy both germs and poisons. This small word "how" is a far reaching one, for it is upon our ability to meet its mandates that the standard of therapeutics as a science depends.

How then does any agent enhance the defensive powers of the body? Are we supplied with a mechanism which enables us to ward off disease—a mechanism whose activity we can enhance at will? This is the dominant problem that my labors have aimed to solve; they showed that such a mechanism does exist, and that it is built of a set of small organs regarded by Brown-Sequard as the producers of internal secretions, but the functions of which had remained obscure, namely: the pituitary body, the thyroid gland (including the parathyroids), and the adrenals which jointly form what I have termed the "adrenal system."

A brief review of the role of each of these organs is necessary before the action of drugs upon them can be defined.

The *pituitary body* is one of those unfortunate structures which histologists and physiologists relegate to the waste basket as "vestigial organs" when they can not explain its functions. It is fortunate, in fact, that it is located below the brain, beyond the reach of surgeons, for there would have been a holocaust of pituitary bodies just as there has been a holacaust of appendices, ovaries, etc., unless resort to surgery had been checked by the appalling results of such a procedure. Indeed, when this organ is completely removed in adult animals, formidable symptoms ensue: the temperature and the blood-pressure recede; nutrition is inhibited, as shown by rapid emaciation, the intense weakness and lowered metabolism. Dyspnoea, muscular co-ordination, intercepted by convulsions, follow, and, usually on the third day, the animal lapses into coma and dies. Conversely we find the pituitary causing opposite phenomena when it is the seat of hyperaemia, hypertrophy, or tumors which render it overactive. In the early stage of acromegaly, for instance, the general nutrition and muscular power are greatly increased. The overnutrition is such, in young subjects, that their stature often reaches that of giants.

The importance of the pituitary to life is further emphasized by the fact that the morbid symptoms and death caused by its removal, do not follow removal of the brain. As shown by the Cornell frog, Goltz's dog, and other examples, all the functions other than intelligence, are, after recovery, as perfectly performed as if the cerebral hemispheres were still present.

How does the pituitary so prominently influence the temperature, the blood-pressure, metabolism, and nutrition, all functions which affect the entire organism?

Is it through the intermediary of a secretion as generally believed? Not a single proof is available in literature to show that the pituitary body secretes anything. There is ample evidence, however, contributed by such men as Cajal, Andriezen, Gentes, and others, to show that the pituitary is connected by nerves with the base of the brain. My researches showed, moreover, that these nerves were the beginning of a nerve-path which, passing by way of the bulb, the spinal cord, the upper sympa-

thetic ganglia, and the splanchnic terminated in the adrenals. Not only did excitation or division of this path at intervals produce the identical phenomena observed after removal, excitation, or disease of the pituitary body, but the same procedures applied to the adrenals also provoked the same phenomena. Briefly, I found the pituitary body and the adrenals were united by nerves, and that it was through the adrenals that the pituitary produced the various phenomena credited to it.

It becomes a question now as to how the adrenals awaken these remarkable effects.

Physiologists had been unable to discover the identity or source of an "internal secretion" shown by Bohr and other physiologists to be necessary to explain pulmonary respiration, in so far as the taking up of oxygen from the air was concerned. They had, admittedly also, failed to find the origin of 96 per cent. of the substance which distributes oxygen to all the tissues, the haemoglobin. My investigations showed that it was the secretion of the adrenals which fulfilled both these functions. Being secreted into veins which opened into the inferior vena cava, it inevitably reached the lungs; being a powerful reducing agent it necessarily absorbed oxygen on being exposed to the air of the air-cells. Moreover, the previously unidentified albuminous component of haemoglobin gave all the reactions of the adrenal secretion. A striking confirmation of the latter fact was recently contributed by Professor Mulon, of Paris, who found that the red corpuscles gave all the reactions of adrenalin.

The manner in which the adrenals awaken the various phenomena previously enumerated may now be accounted for. As their secretion is the substance which supplies oxygen to all tissues, their removal causes a lowering of the temperature and of the blood-pressure, arrest of nutrition, emaciation, great muscular weakness, and death—precisely the symptoms that follow removal of the pituitary body, the seat of their center. Conversely it explains how adrenal extract or adrenalin raise the temperature and the blood-pressure, *i. e.*, by enhancing oxygenation and metabolism in all tissues. The remarkable influence of the adrenals on life—in keeping with that of the pituitary body—

is not only shown by the fatal effects of their removal, but also by the direct action of their products in sustaining life. As is well known, Crile, by means of injections of adrenalin in saline solution, was able to resuscitate animals fifteen minutes after all signs of life had ceased, and to keep a decapitated dog alive ten hours.

On the whole, the pituitary body through its connection with the adrenals governs the pulmonary and tissue respiration; that is to say, the life process itself.

The pituitary body regulates the functions of another set of organs: the thyroid gland and its glandules, the parathyroids. The nerves from the pituitary to these organs were discovered by de Cyon, a Swiss physiologist, who pointed out that they caused dilation of the thyroidal vessels, increasing, thereby, the functional activity of these organs.

The *thyroid and parathyroids,* in the light of my researches, play an important role closely related to that of the adrenals. The purpose of their secretions, acting jointly, is to increase the vulnerability or sensitiveness of all tissues, waste-products, bacteria, etc., to oxidation, by enhancing directly the inflammability of their phosphorus. In other words, it causes all these bodies to burn faster under the action of the oxygen-laden adrenal product, the albuminous haemoglobin. The efficiency of the latter, and the activity of metabolism in all tissues, is thus dependent in a great measure upon the presence of thyroid secretion of the blood. Important in this connection are the facts that owing to their high content in phosphorus, all nervous elements, including the nerve-centers, are especially sensitized by thyroid extract, and that their functional activity is correspondingly enhanced. The adrenal centers being subject to this action as all other centers, the thyroid secretion activates metabolism in two ways: (1) by increasing the inflammability of all cells, and (2) by exciting the governing center of general metabolism, that of the adrenals.

The wonderful action of thyroid extract in cretinism now becomes self-evident: the stunted stature recalls inactivity of the pituitary (overactivity of which, we have seen, breeds

giants) and inadequate secretory activity of the adrenals. Thyroid extract causes the cretin to grow rapidly. This is evidently due to increased oxygenation since the temperature previously low, now rises to normal and often beyond. There is, indeed, a greater intake of oxygen, a greater output of carbon dioxide, and increased excretion of nitrogen—all proofs of enhanced metabolism. Every function, every structure, including the skin and hair, shows evidences of development and growth. The nervous system outstrips them all, however—owing to its wealth in phosphorus, we have seen; as a result the mental capacity improves, and ultimately, a normal average child is evolved from the idiotic dwarf that was.

This brings us back to the main subject of this address: therapeutics; but therapeutics relieved, in respect to the action of adrenal and thyroid preparations, and also, I may add, of iodine and its salts—of the odium of empiricism. We can now say HOW *adrenalin,* for example, acts. On entering the blood, it increases its oxygenizing power, as if a temporary exacerbation of activity of the adrenals had done so; hence its fleeting action. Of *desiccated thyroid* we can also say: it adds to the blood constituents of the thyroparathyroid secretion, which not only increases the inflammability of the cellular phosphorus under the action of the blood's oxygen, but in doing so it increases incidently the functional activity of the adrenal center, and therefore, the oxidizing power of the blood. Both conditions of perfects metabolism being met, the whole organism is endowed with new life when the doses are small but too rapidly consumed when the doses are large.

Moreover, this furnishes the clue to the action of *iodine and its salts,* which, although their action we have seen, is admittedly unknown, are so valuable in practice that, as stated by Manquat, physicians use them when they are at their wits' ends. As is well known, thyroid extractives become inert when the iodine they contain is abstracted; it is at least in part to this haloid, therefore, that its owes its action. Iodine and its salts act much as do thyroid preparations, therefore—a fact confirmed in practice—but less actively, owing to the absence of the other com-

ponents of the thyroid secretion, which give them, as suggested by Notkin, the character of a ferment.

The practical feature in this connection is that thyroid extract is capable also of increasing the power of the blood to destroy germs and their toxins. Gruber long ago urged that the defensive constituents of the blood were internal secretions; Wright holds a similar view concerning the opsonins; but neither of these distinguished investigators discovered their source. Now my own researches have shown that *opsonin* gives the reactions of the thyroparathyroid secretion; that the oxygenized adrenal secretion, that is to say, the albuminous constituent of haemoglobin, is Ehrlich's *amboceptor,* and that the main constituent of his complement is *trypsin,* the identical ferment through which, according to Metchnikoff, phagocytes kill and digest bacteria.

The process through which a thyroid preparation increases the autoprotective activity of the blood now suggests itself: it increases directly the opsonin which sensitizes what bacteria, toxins, toxic wastes, etc., may be present. By enhancing simultaneously the metabolic activity of all tissues, including the adrenal center, the pancreas and the phagocyte-producing organs, it thus endows the blood, the lymph, and the lymph glands with an excess of their bacteriolytic and antitoxic substances and cells, insures their destruction, and, at the same time, their conversion into eliminable end-products.

This introduces a feature of therapeutics which is at present absorbing the attention of the whole scientific world. How do Koch's tuberculin, Wright's vaccines, Coley's toxins, etc., produce their beneficial effects? Wright stated four years ago, referring to the protective agents of the blood, that if pathologists "knew the laws by which such substances were produced," they could "call forth a production of those substances."

I suggested several years ago that the anterior lobe of the pituitary body was not, as now believed, a secreting structure, but a sensitive organ which perceived, as it were, any poisonous substance that happened in the blood. I traced this organ throughout the entire animal scale down to such low forms as Mollusks. Zoologists having concluded that its purpose was to

test the water ingested by these lowly animals for noxious substances, they gave it the suggestive name of *test-organ* or *osphradium*. My opinion that this organ exists in the higher animals was confirmed in Europe recently, Gentes having found histologically in the pituitary, a sensory structure similar to that of the olfactory membrane, a fact which suggests clearly its purpose: to detect the presence in the blood circulating over it, of any poison that it may contain, just as the organ of smell enables us to detect malodorous emanations which compromise the purity of the air.

The manner in which tuberculin and other bacterial poisons produce their effects will now appear. On entering the blood they circulate throughout the entire body, including the pituitary body and its test-organ. Now, this structure proved histologically to be the sensitive surface—in the sense that the nasal olfactory membrane is a sensitive surface—of the adrenal center, or, better, the adreno-thyroid center, from which arise both the nerve-path, which I have traced to the adrenals, and the nerves which Cyon traced to the thyroid. On the other hand many investigators have found that during the course of infectious diseases—due therefore to bacterial toxins—the thyroid and the adrenals presented the characteristic signs of excessive functional activity, while the fact that these organs serve to destroy blood-poisons has been known ever since almost their functions have been studied.

On the whole, evidence from various directions points to the sensitive test-organ and its adreno-thyroid center as the structure excited by tuberculin, Wright's vaccines, Coley's toxins, etc., and to the adrenals and thyroid, which the adreno-thyroid center excites, as the organs which supply the blood with bacteriolytic and antitoxic substances, to which I will refer, henceforth, as "auto-antitoxin," its composition being, as I urged several years ago, the same as that of antitoxin.

The strength of this interpretation is sustained by the fact that the reaction produced by tuberculin and other bacterial vaccines corresponds with that caused by excessive functional activity of the adrenals and thyroid. No one, for example,

denies that excessive oxidation underlies the production of fever, and no one will deny that fever, up to a certain limit, is a protective process; but "even if we grant," as Lazarus Barlow wrote recently, "that fever is beneficial, we are completely ignorant of the manner in which it acts." One can hardly realize that so commonplace a symptom should not as yet, with the enormous aggregate of scientific facts available, have been explained. The cause of this now suggests itself: neither fever or any other phase of the immunizing process could be elucidated before the adrenal system, that is to say, the pituitary body, the adrenals, and the thyroid, had been found to fulfill the functions I have described, particularly oxidation.

Essential in this connection is the fact that tuberculin and other bacterial vaccines are used as *remedies*. Interpreted from my standpoint: bacterial vaccines are beneficial, in a given disease, when they increase the efficiency of the body defenses in the manner described. But an important question imposes itself at this point, one bearing particularly upon the branch which interests us all, pharmacology. Can we, with our drugs, also enhance the efficiency of the defensive functions? Let me recall the fundamental principle I have previously urged, that *immunizing medication is the foundation of rational therapeutics.*

And this principle has borne fruit. A letter from an extremely competent and conscientious Virginia physician, Dr. C. F. Brower, received as these lines were being written, may be used to exemplify the tenor of others received: "My results are astonishing to me; and, to my assistant" (who was not as yet familiar with the newer conceptions), "they are astounding and incomprehensible." This refers to results obtained with the most familiar remedies of our pharmacopoeia—to a therapeutics in which we can govern the efficiency of our defensive mechanism, just as an engineer can regulate the speed of a locomotive through the throttle valve—a therapeutics, in other words, in which our intelligence, and not empiricism, holds sway.

This does not mean, of course, that our resources are limited to fighting bacteria and the effects of their toxins, toxic wastes, and other poisons. They include the use of measures to counter-

act insomnia, pain, and other distressing symptoms, and also morbid developments in the course of disease such as cerebral or pulmonary congestion, paralyses of function, etc. To make this clear, I will close my remarks with a brief outline of the two or three main effects through which a few groups of drugs, tonics, analgesics, hypnotics, etc., counteract these morbid phenomena, referring you to the work previously mentioned for the action of other groups, a review of which would too greatly prolong this address.

A few explanatory facts are needed to facilitate your understanding of the principles I am about to submit: 1. The adreno-thyroid center, we have seen, receives the impulses it transmits to the adrenals and thyroids from the sensory test-organ, which resents, as it were, the presence of a poison in the blood, and awakens the protective reaction. To simplify the explanation of the mode of action of the drugs which evokes this defensive process in the blood, I will only mention the adreno-thyroid center, taking it for granted that you will understand that it is the sensitive surface of this center, the test-organ, which is primarily excited by the drug. 2. Not all drugs stimulate this organ; some depress it or anaesthetize it more or less actively, as will be shown presently. 3. Notwithstanding the fact that most drugs, in therapeutic doses, act primarily upon one or more centers, each drug acts specifically; that is to say, in a manner peculiar to that drug alone, or to the group of drugs to which it belongs.

In the case of one group of agents, those which provoke, through their action upon the adrenal system, the appearance in the blood of an excess of auto-antitoxin, a new term became necessary. That of "antitoxigen" appears to me to convey the intended meaning.

Antitoxigens.—The most active antitoxigens in infections and intoxications include some of the drugs now known as alteratives, the physiological action of which, we have seen, has remained obscure. *Thyroid* preparations are very active in this connection since they provide the blood directly, as previously explained, with an excess of opsonin to sensitize the bacterial toxins and

other poisons. At the same time, by exciting the adrenal center, they incite the production of the other constituents of auto-antitoxin, and the genesis of phagocytic leucocytes. *Iodine* and the iodides act in the same way, but they provide less opsonin, since they only supply the thyroid and parathyroids with the main agent which enables these organs to increase their production of this sensitizing body. They are therefore far less active, in this particular, though they compensate for it, in a measure, but exciting more actively the adreno-thyroid center, thus enhancing oxidation to a greater extent. *Mercury* is well known in this connection, as the widespread use of calomel attests. Its salts act by exciting powerfully the adreno-thyroid center, thus providing the blood more evenly, as it were, than the two preceding agents, with all its defensive constituents. Their well-known action on the liver (since this is the organ in which the antitoxic process is most active) and in infections, especially syphilis, is due to this property.

A remarkable agent in this connection is *creosote,* so effective in pulmonary tuberculosis and pneumonia when judiciously used. Not only does it promote the formation of auto-antitoxin and phagocytes by exciting the adreno-thyroid center, but it depresses the center which regulates the caliber of the arterioles, causing these small vessels to dilate. As a result an excess of blood is admitted into all capillaries, including those of the diseased area, and as this blood is unusually rich in auto-antitoxin and phagocytes, the pathogenic bacteria and their toxins are vigorously attacked.

The solvent property attributed to alteratives is readily explained by the action of the opsonin or thyroid secretion which they directly or indirectly add to the blood, the increased inflammability of the phosphorus contained in morbid products, gummata, for instance, rendering them more amenable to the digestive action of the auto-antitoxin. This property, when exaggerated, becomes a source of danger, when too large doses of either of the above remedies are given, since the red corpuscles and the tissues themselves may then undergo dissolution—observations borne out by the familiar terms "haemolysis" and "autolysis."

Again, fever, we have seen, is due to a more or less marked increase of the auto-antitoxin in the blood, but if it exceeds 105 degrees F. to any great extent, the bacteria are not only dissolved, but the red corpuscles are also exposed to dissolution.

Tonics.—The most active of these remedies also excite the adreno-thyroid center, but only sufficiently to enhance general nutrition. Practically all these agents, however, influence another center at the same time, usually the vasomotor center. *Strychnine* is one of these, though it does not excite the adreno-thyroid center as actively as do mercurials, by stimulating also the vasomotor center, it causes general vaso-constriction, and by thus driving the enriched blood into the tissue capillaries increases general nutrition. The beneficial action of *digitalis* in heart disorders is due to a marked stimulating action on the adreno-thyroid center. It also excites, however, the sympathetic center (to be described presently), which not only governs the caliber of the arterioles, but causes these vessels to propel the blood into the capillaries, and to increase thereby the nutrition of all tissues, including the heart-muscle. Its powerful action on the adreno-thyroid center causes the adrenal secretion to be produced in considerable quantity when large doses are given; as this secretion serves also, as I urged several years ago, to aid the contractions of the right ventricle, an excess of it causes the latter to contract with greater vigor than the left, the pulse becoming dicrotic, as noted by various authors. *Strophanthus, apocynum, convallaria,* and other heart tonics act in a similar way, but with less vigor.

Quinine, on the other hand, acts indirectly. It does not excite the adreno-thyroid center, but the vaso-motor center. In large doses it causes such violent general vaso-constriction that the blood is forced into the peripheral capillaries, the brain, the ears, the conjunctiva, etc. Hence the headache, the tinnitus, etc. It protects against malarial infection by driving an excess of blood (including what auto-antitoxin it happens to contain) into the skin, thus augmenting the resistance to infection by the mosquito. Its curative power is due, as is well known, to its direct toxic action upon the plasmodium.

Hypnotics.—The most active of these agents, that is to say, the true hypnotics, produce their action by markedly depressing the adreno-thyroid-center. This is the action of *chloral hydrate,* for instance. As metabolism is thus slowed in all tissues, including the muscular elements of the arteries and veins, these vessels dilate and the blood recedes into the larger trunks, especially those of the splanchnic area. The volume of blood in the brain being reduced, sleep follows. *Paraldehyde, sulphonal* and *trional* act in the same way, the two last-named, however, with greater violence, as shown by the cyanosis they sometimes produce—a self-evident sign of deficient oxygenation, the function over which the adrenals preside. The *bromides* are less efficient as hypnotics; but this is because they do not depress the adreno-thyroid center when given in anything except large doses. They depress the vaso-motor center and cause sleep, as does chloral, by causing general vaso-dilation and recession of blood from the brain.

Analgesics.—The cause of the prevailing obscurity as to the manner in which these agents relieve pain, is explained by the fact that the functions of the nerves through which they do so has also remained obscure. Although the vaso-motor center is located in the bulb, electrical stimulation of the pituitary body, as shown by Cyon, Masay, and others, causes an immediate rise of the blood-pressure. I found that this was due to the presence in that organ of a center, the search for which had been abandoned many years: that of the sympathetic system; and moreover that its purpose was to govern the propelling power of the arterioles which admit arterial blood into all capillaries. With this fact before us the action of analgesics becomes self-evident. *Antipyrin,* for example, relieves pain because it excites the sympathetic center in the pituitary and thereby causes excessive constriction of the arterioles; the volume of arterial blood circulating in the sensory terminals of the diseased area being reduced, the pain ceases. That this mechanism is the true one is shown by Sawadowski's observation that a section across the basal structures, that is to say, between the pituitary and the bulb, causes antipyrin to lose its action. *Acetanilid* and other

coal-tar products act in the same way. So do *opium*, *morphine*, and other opiates. The hypnotic action of large doses of the latter agents is accounted for by the same process: the cerebral arterioles being also constricted and less blood circulating in the brain, sleep is produced.

Anaesthetics.—These agents differ totally from either hypnotics or analgesics in the manner they produce their effects. Chloroform, by exciting violently the vaso-motor center, first causes general vaso-constriction, and by thus driving an excess of blood forcibly into the capillaries of the cerebro-spinal system, produces the first stage of anaesthesia, that of excitement. True anaesthesia occurs when the vaso-constriction of both arteries and veins becomes sufficient to produce stasis of the blood in the cerebro-spinal capillaries, and to cause it to become prematurely venous: the functions of the brain being in abeyance, sleep and anaesthesia follow. The action of *ether* differs from that of chloroform only in that it does not excite the vaso-motor center as violently. *Nitrous oxide* produces anaesthesia by preventing the access of air to the venous blood and the adrenal secretion it contains while passing the air-cells: the adrenal secretion having failed to become oxygenized by the alveolar air, does so at the expense of the circulating blood after passing the alveoli. Hence the immediate cyanosis and the rapidity of the anæsthesia, the entire cerebro-spinal system being supplied with blood deficient in oxygen.

Vaso-Cardiac Depressants.—Veratrum viride, the most important of these agents, produces its effects by depressing markedly the vaso-motor center. All the vessels of the body being dilated, the blood recedes from the periphery to the deeper and larger vessels, excessive arterial tension and the resulting resistance of the blood-column to the heart's contractions are counteracted. This is the only remedy whose physiological action has, in my opinion, been known. *Aconite* produces its effect by depressing the sympathetic center, thus causing dilation of the arterioles and the penetration of an excess of blood into the capillary system. When large doses are given this capillary

hyperaemia excites the peripheral end-organs of sensibility and tingling is caused, besides flushing, headache, etc.

These few examples must suffice to sustain the impression I hope to convey, that if, as stated by Professor Sollmann, therapeutics is now not even an art, but "a confusion," the painstaking labors of a host of investigators have afforded us all the factors necessary to at least elaborate a foundation for a system in which simplicity and precision supplant confusion. Indeed, I must emphasize the fact that although the action of each drug, as I interpret it, is devoid of complexity, it is based on a vast array of evidence—all of which converges towards the solution I urge. The action of mercury for instance, is sustained by the recorded results of seventy-seven experimenters—to say nothing of the clinical data adduced.

Permit me to add that notwithstanding this simplified pharmacology, it is possible to select accurately the remedy that will meet the determining cause of a disease in its own field and, more than ever before, counteract its morbid effects. What may we not hope when, with your aid, our knowledge, from the mere rudiments I have to offer, will have reached a high degree of perfection? Not only will therapeutics have attained its merited position as a science, but it will have raised medicine itself to so high a plane in the public estimate that no one will even think of trusting health and life to any man or woman other than a scientifically trained physician.

Abstracts.

NON-SURGICAL TREATMENT OF CHOLELITHIASIS.

Ludwig Woelfert, M. D., Brooklyn, N. Y., writes in the International Journal of Surgery, March, 1908, on "The Non-Surgical Treatment of Biliary Affections." There is a class of cases which shows typical symptoms of cholelithiasis, without colic, and in which differential diagnosis from simple cholangitis can not be made with absolute certainty. There is perhaps a small

but steady absorption of biliary secretion into the circulation, and occasional execerbations manifest themselves by jaundice. A corresponding insufficiency or deficiency in the quantity or quality of bile causes a continuous disturbance of the digestive tract. Constipation exists, and there may be diarrhea from excessive putrefaction, consequent destruction of erythrocytes, with anemia and its train of symptoms—neuralgias, headaches, visual disturbances, dizziness, emaciation. The bile absorbed into the circulation facilitates diapedesis of the erythrocytes through the capillaries and may even cause their complete emigration. There may be capillary hemorrhage from any mucous surface, and it may even be subcutaneous.

The one common diagnostic feature is that the urine exhibits abnormal contents of chromogens and of indoxyl and skatoxyl derivatives. The following test which I have devised and which is sharp, reliable and quickly made, will be found useful:

Four to five c. c. of urine are mixed with an equal volume of hydrochloric acid; a dark red or purplish color reaction indicates an excess of skatoxyl. About one c. c. of chloroform and one-half to two drops of liq. sod. chlorin. U. S. P. are then added, and the mixture is shaken for a few seconds; the appearance of the blue reaction of the chloroform, which may vary from the least tinge to the deepest indigo, shows indican. Upon heating, the indigo is gradually converted into its isomeric red modification, the chloroform thereby changing from blue to purple and red. This change of color is also seen with other indican tests, the rapidity with which it occurs depending much on temperature and strength of reagent. Excess of liq. sod. chlorin. discolors the chloroform. In the supernatant liquid the nature of the chromogen or chromophore may be observed by its color, which may be anything from yellow to black. The study of the significance of these various colors offers a field for further investigation. Of course medicines taken by the patient may modify the color reactions.

Excess of indoxyl and skatoxyl does not per se indicate disturbances of the liver or its appendages; there may be gastric dilation, cancer or ulcer, affections of the pancreas, duodenum

or ileum, mixed tubercular infection, or suppurative processes anywhere. Skatoxyl and its congeners predominate in affections of the large intestines. But when associated with the subjective difficulties enumerated above, biliary disease can be diagnosed with certainty.

Catarrh in the biliary system on the basis of bacterial invasion and stasis of the portal circulation, furnishes medical indications. Presence of stones does not necessarily demand operative procedure; stones are often found at autopsies of subjects who never had the least symptom of biliary trouble. Appropriate medicinal means can often place stones into a state of harmless latency, or possibly put the viscus into a condition to eliminate them, by stimulating the formation of so much thin bile that the stream becomes powerful enough to expel the calculi, their mobilization being favored by re-establishing normal conditions in the ducts.

I resort to the usual dietetic and hygienic measures and to the use of biliary antiseptics and stimulants and analeptics. That a combination of salicylic acid, sodium oleate, phenolphthalein and menthol is effective, I know from my experience with the probilin pills of Bauermeister. I use them whenever my urinary test gives positive result, including hepatic and gastrointestinal cancer—for symptomatic benefit—and anemia due to bile absorption. I have just discharged, after three months' use of the pills, a very obstinate and marked case with symptoms of choleic disorders dating back as far as twenty years. She had for a number of years drifted from one specialist to the other, her normal ovaries having been finally removed without relief. She took two pills twice daily with hot water, and later four pills twice daily. At the time of writing she is greatly improved, free from distress, and the anemia is yielding, now that normal bile flow is restored.

Records, Recollections and Reminiscences.

SPECIAL NOTICE!

The 18th Annual Re-Union, U. C. V., will be held in Birmingham, Ala., Wednesday, Thursday and Friday, June 9th, 10th and 11th, proximo, and the Eleventh Annual Meeting of the Association of Medical Officers of the Army and Navy of the Confederacy will be held at the same time and place. Members who wish to present papers, essays, etc., will kindly notify at an early date, the Secretary of the Association, Dr. A. A. Lyon, State Capitol, Nashville, Tenn.

The meetings of the Association of Medical Officers will be held in the rooms of the Commercial Club, opposite the Court house on 21st st., between 2d and 3rd Avenues, to which all members and those who desire to become members are requested to come immediately on reaching the city.

The Jefferson County Medical Society, the second largest in the State of Alabama having extended a most cordial invitation to the Association to meet in Birmingham, a most satisfactory and enjoyable meeting may confidently be expected.

IN CASES OF FRACTURE OF THE SKULL, one should wait for focal symptoms before operation, as a linear fracture without depression is often not followed by serious results. On the other hand, no time should be lost in raising a depressed piece of bone or exploring the skull for hemorrhage when *any* focal symptom presents itself.—*American Journal of Surgery.*

Editorial.

COMMENCEMENT EXERCISES OF MEDICAL DEPARTMENT, UNIVERSITY OF TENNESSEE.

The annual commencement exercises of the University of Tennessee Medical Department were held in Watkins Hall in this city on Thursday evening, April 30th, ult. A large, appreciative and interested audience completely filled all the seats, many were standing and a number failed to obtain entrance. The faculty occupying the stage and the graduating class the seats immediately in front. Pelletieri's orchestra furnished a number of pleasing musical selections during the evening.

The execises were opened with an invocation by Rev. Dr. E. C. Atkins; the "charge" to the graduates was delivered by Prof. T. Hilliard Wood, M.D., which will be found in full in the first part of this issue. Judge J. W. Judd was then introduced and delivered an excellent address in which he dealt with the medical profession from its inception to the present. He gave the class many good words of cheer and advised as to their future life-work.

Professor Brown Ayres, Ph.D., LL.D., President of the University, then conferred the degree of "Doctor of Medicine" on the following graduates: R. P. Aldridge, Kentucky; W. P. Allen, Alabama; Jno. R. Avants, A. L. Bardill, C. W. Brabson, Tennessee; E. A. Bickley, Louisiana; L. J. Caldwell, Q. C. Cantrell, Tennessee; L. L. Carpenter, Pennsylvania; Wm. L. Davis, R. L. Dossett, O. S. Deathridge, Tennessee; Wm. N. Elkins, Louisiana; J. H. Farrar, C. A. Gardner, H. A. Gilliam, Tennessee; C. A. Grant, Alabama; Chas. Griffith, Tennessee; R. L. Hamilton, Texas; H. A. Hannings, Tennessee; T. F. Harris, Texas; W. A. Howard, Tennessee; J. H. Hunter, North Carolina; O. M. Laten, Jno. H. Lee, Tennessee; J. M. Matkins, North Carolina; R. L. McReynolds, Tennessee; Jno. H. Payne, Texas; Wm. A. Reed, Tennessee; Geo. F. Roberts, South Carolina; W. B. Russell, Kentucky; Cullom Sidwell, J. A. Scott, Tennessee; F. A. Shepard, North Carolina; M. E. Thompson, H. H. Thomas, M. M. Wagner, Tennessee; Jas. E. Walker, Alabama; J. B. Webb, Tennessee.

Prof. T. F. Dunn, M.D., next awarded prizes to the following "Honor Men:" First, Jno. M. Lee; Second, L. J. Caldwell; Third, O. M. Laten; Fourth, J. B. Webb; Fifth, Horace Farrar; Sixth, G. F. Roberts; Seventh, H. V. Hennings; Eighth, L. A. Thompson.

Following are the hospital appointments: Nashville City Hospital, John M. Lee and Horace Farrar; Davidson County Hospital, L. L. Carpenter; St. Mary's Hospital, Evansville, Ind., W. B. Russell.

THE CINCINNATI SANITARIUM.—We have received the thirty-fourth annual report of this most excellent institution, so long and favorably known to the medical profession. From it we learn that the number of patients admitted during the year was 208, of whom the recoveries amounted to 39.9 per cent. The total number treated during the year was 300, of whom 83 were discharged recovered, 84 improved, and 27 unimproved; with only 10 deaths. This number of recoveries and low death rate is still one of the especially marked features of the institution, furthermore, the cases treated were not "selected" for admission on account of mildness or supposed curability. The policy pursued heretofore is still maintained, and after a suitable opportunity for a careful examination and study of a patient, a full and candid opinion as to probable duration and possibility of recovery is given.

Dr. F. W. Langdon is the Medical Director, with Dr. B. A. Williams, who has been so many years in the institution, as Senior Resident Physician, and Dr. Chas. B. Rodgers, Junior Resident Physician, assisted by a full and ample corps of experienced, capable and well trained attendants. The grounds and buildings are suitable, well arranged and supplied with all appliances and essentials.

One of the pleasant features in the history of this Sanatarium is the return after recovery of many patients, to express their gratitude for benefits received.

LONGEVITY AND—"BUTTERMILK."

Long life and how to attain it has an attraction to all of us, and any approach to a solution of the question will ever be of more than passing interest to the mind of finite man. Life, systemic or molecular, is dependent on the proper performance of certain functions; so death, whether a result of disease, violence, or senile decay, is due ultimately to a cessation of one or more of these functions. The heart with its blood-vessels, arteries, capillaries and veins; the lungs with their tubes and air-cells; the brain, including the ganglia and nerves, constituting the great tripod of life, a permanent failure on the part of one soon limiting the activities of the others, and although we have to a great extent followed the classification of Bichat and speak of death beginning at the heart, the lungs or the head, yet in man at least, material impairment of other functions such as those of the skin, kidneys, liver and other glands, as well as the spleen and ductless glands, other tissues and viscera, have a very positive effect in cutting short the brittle thread of our existence.

While we have but one way of beginning life, we have many ways of ending it. Living things with which we are cognizant all grow old and

die; this is a fate as universal, as definite and certain as that a stone thrown into the air will fall back again to the earth's surface. A dog will live for ten or twelve years, a horse for twenty-five or thirty, and a man for "three-score and ten," and "peradventure he may reach four-score;" but we are well aware that no portion of the living substance of either has remained actually the same throughout the time; the chemical elements, atoms and molecules that constituted the living being at the beginning of life have been replaced from time to time, by others brought in with food; and what has remained unchanged throughout the life of the individual has been a form of activity on the physiological side, resting on a base of practically definite composition on the chemical and morphological side. This is the great distinctive feature of living matter or life, and is expressed in the single term assimilation, or nutrition, waste and repair, a property which most distinctly separates living from dead matter. Living matter alone has the creative power of converting dead matter into living substance like itself. Throughout the life of the individual there is a steady stream of dead matter flowing in to be built up into living form, and an equally continuous outflow of dead material that has once been in living form, resembling as Huxley said, "an immense whirlpool, with its ever-changing atoms and particles making up its unchanging form." Spencer, in his "Principles of Biology," defines life as the continual adjustment of internal to external relations, consequently perfect correspondence would mean eternal existence, and if the organism could adapt itself to every change of environment, old age and death would be impossible. This, so far as observation goes, is impossible, and the concensus of belief, which if not universal, is well nigh so, is that every organism and every bit of living matter in an organism has a limited duration of life, regardless of how favorable the external relations may be.

With these views it is an interesting point to ascertain, if possible, the greatest age attainable. Leaving out the Biblical statements and those obtainable from ancient history, by reason of uncertainty as to the unit of time, comparatively modern statistics place the maximum between 120 and 180 years, as we now record time. Citing a few instances may not be uninteresting. R. S. Tracy, in the *Century Magazine*, 1902, cites the case of Noah Raby, at the Piscataway poor farm in New Jersey, who was said to be 129; Lady A. Glenesk, in *The Nineteenth Century Magazine*, in 1897, gives an account of "La Mere Girard," who, according to the parish register of St. Just-de-Claix, in France, celebrated the 100th anniversary of her marriage in her 125th year; Pfluger, of Bonn, mentions "one Brawn, who reached the age of 120," although a confirmed drunkard; he also refers to H. Jenkins, a native of Yorkshire, England, who died at the age of 169, and who, when brought before a justice of the peace to testify to an event that happened 140 years previously, was ac-

companied by his two sons, aged respectively 102 and 100; Harvey, in the third volume of "Philosophical Transactions," gave the results of a post-mortem and an account of the life of Thomas Parr, of Shropshire, who died at the age of 152 years and nine months, having married a widow when he was at the age of 120; and if we may trust the accounts of his life on record, Kentigern or St. Mungo, founder of the Cathedral of Glasgow, reached the age of 185. Sir C. Brown, in the *Br. Med. Jour.*, 1891, states that in 1889 the deaths of 76 reputed centenarians were reported in England and Wales. Our own eleventh census, in giving the total number of deaths of males at known ages, occurring in the year preceding May 31, 1890, as amounting to 458,992, of whom 20,103 had reached the age of 80 and over; 811 of whom were 95 and over. Finally, the 12th U. S. Census for the year ending May 31, 1900, gives the total deaths of all known ages 1,039,094; males, 551,611, females 487,483; 80 years old and over, males 17,525, females 16,261; and that 2,721 attained the age of 95 and over, of whom 1,045 were males, and 1,676 were females.

That longevity is greater among women than men is shown by the last (12th), as well as preceding census reports; the Massachusetts tables of expectation of life give for women at 75 years of age an expectation of 8.29 years; and for men only 7.37 years; the English tables, according to Dr. W. Ogle vary somewhat from this, being for women 6.87, and for men, 6.34. The influence of race, social condition, occupation, and other extrinsic and intrinsic relations have a material effect, however, the most marked of all is heredity, so far as has been ascertained by statistics.

The evolution of a human being has been described as limited to three stages, and that living beings were born, grew and died; but there is another stage that should not be left in the shade, the period of decline, that to which although all the intrinsic and extrinsic causes of disease and death have been avoided or overcome, we all inevitably approach; this decline being as necessary biologically as growth. Old age is not a disease, but a phase of life, and the changes occurring are simply a different mode of being, constituting what is truly a physiological stage as is childhood and adult life; and it is important for us to have in our mind that old age has its place in normal existence. It is a period during which, without being a sick man, one has the need of guidance and advice in order that he may not grow old too rapidly or in an irregular manner.

It has long been known that senility leads to atrophy of organs, to their degeneration and sclerosis; and though these changes are but the effects of age, they have long been cited as causes. By both extrinsic and intrinsic relations they may be developed prematurely, and thus cause age before its time. From this we have had the statements made "that a man is as old as he seems," and "one is as old as his arteries." Starting with the evolution of the individual we find when we encounter senility, certain changes which may be grouped according to three principal types:

(1) Pure atrophy of the constitutional elements of the tissues—the "lean and slippered pantaloon," in which we can note a diminution in the size and weight of the different organs. (2) Progressive infiltration into certain tissues of organic or inorganic elements foreign to their primitive constitution—the fatty, albuminoid and calcareous infiltrations. (3) An exaggerated production of connective tissue—there is no question but that an arterial lesion diminishing the nutrition of an organ or tissue will cause a sclerosis of that organ or tissue; but also, as primitive connective tissue is the least differentiated of all tissues and in which the power of attraction is preserved in highest degree, serving as a framework of more highly organized cells, under the pressure of long-continued over-action higher cell production is diminished, as well as in the natural process that inherently belongs to age atrophy, the connective tissue begins to form and in excess with increased development of a lower form of perfectly and clearly specialized fibrous tissue, and senescence has commenced for that organ whether it be after 50, 60, 70, or even 80 years. When connective tissue begins to lose a part of its power of attraction and differentiates, whether pathologically or physiologically, it becomes fibrous tissue and is produced in excess, and that may occur independent of arterial disease—pathologically it is the anatomical substratum of disease, on the other hand, physiologically it is a simple state of being due to natural or normal change.

With the structural or anatomical change along these lines we also have a lessening, a diminution of function along all lines, mental activity, muscular power, secretion and excretion, all move more slowly; possibly the change in the assimilative function being less marked. The old man can yet make active use of his brain, thinks and reasons, but he scarcely uses it at all to learn, he does not acquire new facts and ideas, and lives almost entirely in those previously acquired. His muscular activity is also greatly impaired. His digestive organs, however, continue to discharge their proper functions, and despite a slight diminution, which is manifested especially when an increase of function is accidentally demanded of it, it continues to preside over the elaboration of assimilable products in a manner entirely sufficient for the maintenance of life.

Right here lies one point of danger to the aged—a too-active assimilation, especially if stimulated by a too-strenuous activity, mental or muscular, may bring about in one instance a sudden breakdown somewhere alone the line, or on the other, an increased development of connective tissue. In my early life an old friend, somewhat of a philosophical turn said to me: "An old man is like and old wagon, with a light load, a moderate gait and over a good road it may last a good while and do considerable service; but over-load it, go too fast over a rough road, expose it to all kinds of weather, and you have a breakdown,

and the great trouble is, that you have nothing left to patch to or repair." "*Festina lente*" is and should ever be the watchword as "old age comes creeping on apace."

We will conclude these somewhat random thoughts which have extended beyond our original intention by the following extract from *The Scientific American* of May 16,, referring to a recent translation by Dr. P. Chambers Mitchell, of London, of "The Prolongation of Life. Optimistic Studies," by Elie Mitchnikoff, sub-director of the Pasteur Institute, Paris, published by G. P. Putnam's Sons, which after mentioning the various ages attained by different invertebrates and vertebrates, says:

"Upon inquiring into the causes of these variations in duration of life, Metchnikoff finds the key in the digestive system. The organs of respiration, circulation, and of urinary excretion show no great differences in the various forms of creation. When, however, we reach the digestive tract, the whole aspect changes. This is most markedly shown in birds, for in the various species, the greatest differences in length of life and in the composition of the digestive tract are found.

"As spoken of before, parrots are very long-lived. They have a very simple alimentary canal, and a very small number of intestinal microbes, owing to the short time that matter remains in the intestine. Astriclus and other cursory birds, provided with a well-developed cæcum, show profuse and varied intestinal flora. They approach the short-lived mammals in length of life. If length of life is due to freedom from intestinal microbes, a preventive of bacterial life must be found. This, according to Metchnikoff, seems to exist in lactic acid.

"That lactic acid is a preservative is a time-honored fact. Meat is often preserved in sour milk. Milk itself undergoes lactic fermentation, but it decomposes only under the conditions most propitious for decomposition to take place. Sauerkraut is the product of lactic acid fermentation, and owes its keeping qualities to this substance. The races living upon the various preparations of sour milk are usually found to attain remarkable ages. Cases, both individual and collective, of great age in those living on a diet of curdled milk are almost too numerous to mention. A few, however, may prove instructive. Metchnikoff gives an account of one Riley, who was shipwrecked on the western coast of Africa, and was enslaved by Arabs. He says members of the tribes with whom he came in contact were two or three hundred years old. That these figures are too high is only too probable, nor can they be taken as more than indications, yet they are not without interest, since these Arabs lived upon camel's milk, fresh or soured.

"In Bulgaria there is a surprising number of centenarians; the staple food in Bulgaria is *yahourth,* a soured milk. A laborer of Verdun, Ambroise Jaulet by name, died in 1751, at the age of 111 years. He 'ate nothing but unleavened bread, and drank nothing but skimmed milk.'"

"Curdled milk and other similar milk products are the result of the action of lactic-acid bacilli, which produce lactic acid at the expense of milk sugar. In most of these soured milks there are too many different kinds of microbes, often pernicious, associated with the bacillus actually causing the desired fermentation. Therefore it is best to procure some form of ferment which is known to be pure. The preparations of the Bulgarian bacillus are the best for this purpose, according to Metchnikoff.

"The Bulgarian bacillus was isolated from yahourth by M. Massol. It produces lactic acid in large quantities, while very small quantities of other acids, such as acetic and formic, which are somewhat injurious, are formed.

"The method of preparing soured milk advocate by M. Metchnikoff is as follows: 'After the milk has been boiled and rapidly cooled, pure cultures of the lactic microbes are sown in it in sufficient quantities to prevent the germination of spores already in the milk and not destroyed by the boiling. The fermentation lasts a number of hours, varying according to the temperature, and finally produces a sour curdled milk, pleasant to the taste, and active in preventing intestinal putrefaction. This milk, taken daily in quantities of from 300 to 500 cubic centimeters, controls the action of the intestine, and stimulates the kidneys favorably.'

"The bacilli may also be taken dry as small pellets, but a goodly quantity of sugar-coating material, such as jam or the like, must be taken with each tablet to furnish the necessary material from which the microbes can produce the lactic acid. Metchnikoff claims that he has been himself benefitted by this treatment."

SCIENTIFIC THERAPEUTICS.

We have given a large amount of our space in this issue to the very valuable and most interesting article read before the Philadelphia Branch of the American Pharmaceutical Association, by Dr. Chas. E. deM. Sajous, in the early part of May, 1908, and reprinted from advance sheets of *The Monthly Cyclopedia of Practical Medicine* for May, 1908, of which Dr. Sajous is the editor. We might properly call the article an "abstract" of the views of its able author so fully elaborated in his magnificent work in two large volumes, *The Internal Secretions and Principles of Medicine,* the last volume of which we had the pleasure of noticing in the January number of this journal.

We can most heartily commend the article to the attention of our readers who will find in it much food for careful thought. His views and observations account in a most satisfactory way for a number of problems connected with a correct understanding of scientific therapeu-

tics. The arraignment of latter day therapeutic nihilists, his views of the action of the ductless glands, and the effects of antitoxigens, tonics, hypnotics, analgesics, anesthetics, vaso-cardiac depressants, etc., are most interesting and entertaining, and will well repay the time taken to read carefully and studiously the entire article.

COMPARATIVE POTENCY OF HYOSCINE AND SCOPOLAMINE HYDROBROMIDE IN REFRACTION WORK: EVIDENCE AS TO UNMISTAKABLE NON-IDENTITY.

Dr. Wendell Reber of Philadelphia, contributes an interesting article upon this subject in *The Journal of the American Medical Association,* for April 25th. His paper was read in the Section on Ophthalmology of the American Medical Association at its Atlantic City meeting in June, 1907. For some unexplainable reason this article, which bears so strongly upon the controversy concerning the alleged identity of hyoscine and scopolamine, has been withheld from publication for eleven months. This is of peculiar interest, inasmuch as the editor of the Association Journal, during this period has been asserting and reasserting most vociferously through the columns of that journal that these two alkaloids are both chemically and pharmacodynamically identical. Dr. Reber's conclusions, which were based upon careful experimental work made upon human beings, are diametrically opposed to the assertions of Dr. G. H. Simmons, Dr. H. C. Wood, Jr., and others, in *The Journal of the American Medical Association,* and its "anvil chorus."

Dr. Reber was led to these experiments by an experience reported in *The American Journal of Pharmacy,* in 1899. At that time he found that when one drop of a 1-10-per cent solution of hyoscine hydrobromide was used in the right eye, and one drop of the same strength solution of the scopolamine salt in the left eye of a youth of sixteen with normal eyes, the reaction of the ciliary muscle was decidedly different in the two eyes. This led him to the conclusion that there was a difference of action between the two alkaloids, in spite of their alleged identity.

Following up this earlier experiment, he says, that "within two years three persons were found who were so doubtful about the acceptance of even a plus 0.25 D. sphere (under cycloplegia) as to fit them for these tests." These three persons were a 22 and 26 year old female and a 20 year old male. He accordingly made upon them the same experiments already recorded with the sixteen year old boy some years previously. In the right eye 1-10-per cent solution of hyoscine hydrobromide (Merck) was inserted and in the left eye scopolamine hydrobromide (Merck) solution of the same strength, the solutions being especially

prepared for experimental use by a reliable pharmacist. The utmost care was exercised in order to eliminate all possible sources of error. It was found that the average time of beginning action on the pupil was ten minutes for both drugs and all the eyes. Full dilation of the pupil occurred in thirty minutes with the hyoscine in the two females and in forty-five minutes with the male. (This difference was attributed to the more sensitive sympathetic nervous system in the females.) Under scopolamine full pupillary dilation occurred in forty minutes in the females and in sixty minutes in the male. According to these findings, therefore, the average time required to produce full pupillary dilation under hyoscine was thirty-five minutes in the three cases, and under scopolamine forty-seven minutes.

The effect on the accommodation of each eye was also determined, and it was found that the average time for onset of full cycloplegia under hyoscine in four cases was fifty-nine minutes, while the average time for onset of full cycloplegia under scopolamine was ninety-two minutes. So that, to quote Dr. Reber, "the relative pharmacodynamic power of hyoscine hydrobromide and scopolamine hydrobromide as used in ordinary office work may be said to be somewhere close to 59.92. Or to reduce it to the commoner form of statement, hyoscine in these test cases showed itself approximately fifty per cent more potent than scopolamine in producing cyclopegia for refraction work," and he very pertinently adds, "So much for the academic phase of the matter which seems to be rather at variance with the claims which chemistry makes for these two drugs."

Dr. Reber follows with an interesting study of the chemistry of hyoscine and allied products derived from the Solanaceous plants. He shows that hyoscine hydrobromide and scopolamine hydrobromide were made official in the third edition of the German Pharmacopeia (under the name of the latter), in which they were asserted to be identical "through the influence of E. Schmidt," the authority most quoted by those asserting the absolute identity of these two alkaloids. Apparently this belief in their identity is a one-man dictum which has been passed from Schmidt to the German Pharmacopeia, and thence over to the makers of the U. S. Pharmacopeia.

To show that this difference in action between hyoscine and scopolamine cannot be due to any difference in the purity of the two products, Dr. Reber quotes his correspondence with Merck & Company, to show that both the hyoscine and scopolamine hydrobromide had a rotatory power of -20. In other words, they are chemically identical, of the same degree of purity, yet pharmacodynamically different.

An interesting fact brought out in a letter of Merck & Company is the statement that there are on the market inferior qualities of scopolamine which test only -6 degrees, other products having been

found as low as -2 degrees. This bears out the statement made by The Abbott Alkaloidal Company, concerning the impurity of the commercial scopolamine upon the market.

Dr. Reber says: "This leaves the matter precisly where it was in the beginning, namely: that with two drugs said to be absolutely identical as to clinical effect, pharmacodynamic power, molecular build and reaction with the polariscope, there should seem to be a more or less uniform difference in potency when tested by the delicate accommodation reaction."

He suggests also that there may be a pharmacodynamic difference between other substances which are known to be chemically identical, such for instance as caffeine and theine, cocaine and stovaine; the latter said to be chemical isomers; yet exhibiting wide differences in their action.

"In the last analysis," says Dr. Reber, *"it is always the clinical phase of such studies that interests us most."* With this we most emphatically agree, since in this important report the claims made by Abbott, verified by many practitioners, concerning the non-identity of the action of hyoscine and scopolamine are upheld at every point. Dr. Reber shows that hyoscine and scopolamine differ decidedly in their action upon the eye. If the slightest difference of action of these two substances is admitted the whole argument of the *J. A. M. A.* critics of Abbott must break down. Dr. Reber prefers the hyoscine to scopolamine in his refraction work, just as many others prefer hyoscine to scopolamine when the alkaloids are used for anesthetic or analgesic purposes.

The discussion of this article is interesting, since it bears out the contentions of Dr. Reber in most points. This discussion was taken part in by Dr. Albert E. Bulson, Jr., Fort Wayne, Ind.; Dr. S. D. Risley, of Philadelphia; Dr. Chas. A. Oliver of Philadelphia; Dr. G. H. Price, of Nashville; Dr. Allen Greenwood, of Boston, and Dr. S. L. Ziegler, of Philadelphia. Dr. Bulson, by the way, agreed with Dr. Reber that "hyoscine is more effective than scopolamine as a cycloplegic." This is interesting in light of the fact that Dr. Bulson is the editor of the *Indiana State Medical Journal,* and has reprinted in part and expressed emphatic approval of the attacks upon the H-M-C anesthetic, in which attacks the alleged identity of hyoscine and scopolamine is a most important part of the argument.

Some of those discussing the paper speak of the toxic action of hyoscine, but apparently none of them had made any effort to discriminate between hyoscine and scopolamine. Dr. Reber brought out the point that the worst case of toxemia he had ever seen had resulted from atropine (arrested secretion and excretion).

This paper is one of the most important contributions to the hyoscine-

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